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Research Article

THE ROLE OF THE IMMUNE SYSTEM AND ORAL FLUID AND BLOOD ANTIMICROBIAL PEPTIDES IN PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS

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ABSTRACT

Immunological mechanisms play the leading role in the pathogenesis of inflammatory destructive processes in periodontium. That's why clinical manifestations of chronic generalized periodontitis depend not so much on pathogenicity and virulence of corresponding microflora but on the character of bacterial-gostal interrelations, that is, in many respects - on the degree of macroorganism reactivity, which is determined by the functional state of immune system. Consequently, an important step in understanding the nature of inflammatory periodontal diseases is the study of those immunological factors (cytokines and antibodies) as well as enzymes that can cause shifts in the morpho-functional state of the supporting apparatus of the tooth, as well as cause the corresponding clinic of the indicated pathology.

KEYWORDS

Mixed saliva, patients with GI disease, cytokines and antimicrobial peptide.

INTRODUCTION

Cytokines are protein-peptide factors produced by cells and carry out short-distance regulation of intercellular and intersystem interactions. Not only immunocompetent but also endothelial cells can be producers of cytokines. It has been established that the same cytokine can be produced by different histogenetic cell types, in different organs [1] The functions of cytokines include: regulation of immune response, inflammatory reactions, hematopoiesis, participation in apoptosis, angiogenesis, chemotaxis [3]. To date, the cytokine system consists of more than 300 polypeptide substances. Cytokines of the immune

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system, which are secreted during the implementation of general and local immunity mechanisms, are the most well-studied, showing their activity at extremely low concentrations. These molecules can be considered as mediators of inflammatory reactions, possessing, at the same time, endocrine, paracrine and autocrine types of regulation[5]. In the work of cytokines the phenomena of antagonism and synergy, their interchangeability, as well as pleiotropy, that is, the ability of the same mediator to influence different processes, to act on many types of cells, causing different effects are noted [4]. Interleukins are of the greatest clinical and immunological interest. According to the mechanism of action, these polypeptides can be divided into proinflammatory (inducing an inflammatory response); anti-inflammatory (limiting the development of an inflammatory reaction); and regulators with their own effector functions (cytotoxic, antiviral, etc.) [2]. Since cytokines are mediators of local action - the most indicative and reliable assessment of their concentration in the relevant tissues and natural fluids (e.g., gingival). The diagnostic value of cytokines lies in the fact that the study of their levels allows to judge about the functional activity of different types of immunocompetent cells, the severity and intensity of the inflammatory process, the probability of its chronicity, transition to the systemic level, as well as the prognosis [4]. Cytokine synthesis sharply increases as a result of "tissue stress", i.e., it is an inducible process and practically absent outside the inflammatory reaction and immune response [2]. For example, under the influence of an infectious agent, in particular, lipopolysaccharide molecules, peptidoglycans and muramyldipeptides that are part of the cell wall of Gram-negative periodontopathogenic bacteria, macrophage activation occurs, increasing the production of proinflammatory cytokines (IL-1β, TNF-α, etc.). These cytokines, circulating in the blood, stimulate the secretion of acute phase proteins [6]. In case of late elimination of proinflammatory agent (antigen) and process transition to the chronic form (with increased activity of negative regulators inhibiting inflammation, for example - IL-10) - there will be significant destructive processes. Thus, monocytes and macrophages activated by pathogens synthesize a whole cascade of cytokines, causing imbalance between pro- and anti-inflammatory pool, which, as mentioned above, leads to resorptive phenomena. The study of these processes formed the basis for the cytokine concept of chronic inflammation development, including in the periodontal complex[8]. Pro-inflammatory IL-1β and TNF-α have the most pronounced damaging effect on periodontal tissues. In particular, a direct correlation between the severity of periodontitis and TNF-α level in venous blood has been established [2]. In its turn, IL-1β is one of the main mediators of the generalization of the pathological process in periodontium [9]. Producers of IL-1β are macrophages, to a lesser extent dendritic cells, endothelium and fibroblasts. IL-1β stimulates PMNL emigration from bone marrow, causes exocytosis of lysosomal enzymes and free radicals by phagocytes, stimulates mast cell degranulation, activates prostacyclin production, and hepatocyte formation of acute phase proteins, which is its pyrogenic effect[8]. IL-1β and TNF-α stimulate bone tissue resorption (activate osteoclasts); they adversely affect tissue repair by inhibiting the resynthesis of collagen fibers by fibroblasts; and stimulate collagenase synthesis. Moreover, this activity is manifested at insignificant concentrations of these polypeptides [11]. It was established that with the progression of generalized periodontitis there is a significant increase in the level of these cytokines both in the gum tissues and in the gingival fluid [14]. Moreover, the formed cytokines not only adversely affect the surrounding tissues but also

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stimulate further activation of the cells synthesizing them, which manifests their paracrine regulation [13]. In chronic inflammatory processes in the periodontium (which is especially characteristic of the elderly), there is an imbalance between cytokines, which leads to hyperactivation of osteoclasts. Accordingly, the degree of degenerative and destructive lesions of alveolar bone in generalized periodontitis is directly related to the level of accumulated cytokines [12]. IL-8 belongs to the family of chemokines and is a low-molecular-weight proinflammatory cytokine. Its production is influenced by bacterial endotoxins as well as some cytokines (TNF and IL-1). IL-8 has the ability to activate neutrophils and monocytes, initiating their chemotaxis to the focus of inflammation, can have a destructive effect on bone tissue. Increased levels of this cytokine correlate with acute and chronic inflammatory conditions, tissue neutrophil infiltration. When studying the cytokine profile of periodontitis patients, an increase in IL-8 in venous blood and gingival fluid was also found [7]. In addition, in the pathogenesis of periodontitis and bone tissue resorption an increased secretion of the anti-inflammatory IL-10 plays a special role, which does not allow the development of a complete inflammatory reaction, whose main task is the elimination of the pathogen. As a result, clinically there is a sluggish course of periodontitis against the background of pronounced destructive processes in the periodontal complex [12]. Humoral immunity factors play an important role in the pathogenesis of chronic generalized periodontitis, first of all - antibodies - immunoglobulins that are produced by plasma cells (activated B-lymphocytes) and are specific for a particular antigen. Three classes of immunoglobulins are most associated with periodontal tissues: IgA, IgG and IgM [15]. It was found that immunoglobulins enter the gingival fluid from the bloodstream. Thus, local immunity factors determined in the gingival fluid are the reflection of the general humoral immunity and correlate with it. In turn, the gingival sulcus can be positioned as a peculiar "representative" of the general immunity in the periodontal complex [16]. At the same time, a certain share of immunoglobulins is formed locally, in the marginal periodontal tissues, so the origin of these antibodies determined in inflammation has both systemic and local character [10]. It is established that with the progression of periodontal pathology there is a gradual decrease in the level of nonspecific protection and increase in the activity of specific factors. In particular, in inflammatory destructive processes in periodontal complex there is an increase in immunoglobulin level, which is the result of pronounced antigenic stimulation as bacterial invasion spreads under the gingiva. There is an active synthesis of antibodies, with their subsequent transudation into the gingival fluid[9]. Elevated IgA levels indicate the presence of an acute, or chronic infection (including bacterial origin). Class M immunoglobulins carry out antibacterial immunity and are the first to be produced in response to an infectious factor. Class G immunoglobulins are the leading effectors of humoral immunity. It has been established that the bulk of antibodies to bacteria belongs exactly to IgG [11]. High levels of sIgA, IgG as well as complement fractions are found in the contents of periodontal pockets. In the case of a direct reaction of antibodies with antigens - cytotoxic reactions are observed, which leads to the destruction of tissue structures. It was found that cytotoxic antibodies are most often represented by immunoglobulins of classes G and M [13]. High activity of enzymes - primarily lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) - plays an important role in the development and progression of inflammatory and destructive processes in the periodontal complex [12]. The sources of enzymes in the periodontal complex are host cells (macrophages, PMNL, fibroblasts and

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osteoclasts) as well as plaque microorganisms. The appearance of active forms of enzymes in the gingival fluid initiates the processes of tissue destruction [10]. Lactate dehydrogenase (LDH) is an intracellular, cytoplasmic, glycolytic enzyme that catalyzes the reversible detachment of hydrogen from the lactic acid molecule. Extracellular localization of this enzyme indicates cell death and, accordingly - tissue damage, which is observed when gingival epitheliocytes are destroyed, and the enzyme is released into the interstitium, which leads to an increase in the level of this enzyme in gingival and oral fluids [6]. At the increase of LDH concentration the disturbance of functional activity of a number of immunocompetent cells, neutrophils in particular, as well as the decrease of synthetic activity in tissues are observed [5]. In the presence of periodontal pockets, as well as in the progression of destructive processes in periodontium - a reliable increase in LDH activity is observed, and its increase correlates with the severity degree of periodontitis [3]. 24 One of the most reliable indicators of bone metabolism is the determination of alkaline phosphatase, which catalyzes the detachment of phosphoric acid from its organic compounds. The enzyme is located on the surface of the cell membrane and takes part in phosphorus transport [14]. Numerous histochemical studies confirm the active participation of alkaline phosphatase in bone tissue metabolism. In particular, a reliable increase in the content as well as the activity of alkaline phosphatase is detected in bone tissue destruction [8]. In addition to osteoblasts, this enzyme is found in neutrophil lysosomes as well as in gingival epithelial cells. Moreover, the increase of ALP activity in gingival fluid can be the indicator of destructive processes observed at periodontitis. A direct correlation between the activity of alkaline phosphatase, the level of bone tissue resorption as well as the course of inflammatory processes in periodontium was established [7]. Thus, analysis of cytokine profile, determination of antibodies level as well as enzyme activity in gingival fluid and venous blood of patients suffering from chronic generalized periodontitis is a necessary diagnostic step allowing to estimate the degree and severity of inflammatory-destructive processes in periodontium as well as choose the most optimal, etiopathogenetically justified treatment.

The aim of the investigation was to study immunological features of the mixed saliva in patients with gastrointestinal tract diseases.

MATERIAL AND RESEARCH METHODS

We studied 140 patients with the gastrointestinal tract pathology, of them 98 male (70%) and 42 female (30%), mean age - 51,9 years in the out-patient conditions of Tashkent State Dental Institute in the period of 2020-2023. According to endoscopic examination different gastrointestinal lesions (chronic gastritis; peptic ulcer - gastric and duodenal ulcer) were revealed in the patients. The control group included 25 healthy subjects. Diagnostics of the lesions of various regions of the gastrointestinal tract was based on classical criteria and was carried out taking into consideration clinical, endoscopic, functional, and morphological data The verification of chronic gastritis was performed according to the classification signs, proposed by the International Association of Gastroenterology, with consideration of traditional Russian views, on the basis of endoscopic and morphological criteria. The observation of the patients and healthy patients was performed according to a unified program, which included general clinical examination, esophagogastroduodenoscopy (EGDS). Biomaterial was collected in the morning, on an empty stomach, in graded tubes. In all patients the collection of mixed saliva samples was performed initially before the drug was prescribed. Before the procedure, the

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patient rinsed his mouth with distilled water for 30 seconds, followed by 5 minutes of rest. The patient then swallowed all of the accumulated saliva, after which the direct collection of material began for 15 minutes. When finished, the tube was sealed tightly with a lid, placed in a container with ice, and taken to the laboratory within an hour and a half. In the laboratory, the tubes were centrifuged at 3000 rpm for 10 minutes at 4°C, after which the saliva sample was frozen and stored at -80°C until examination. Pro- and anti-inflammatory cytokines (IL-1, IL-2, IL-4, IL-6, IL-8, IL-10 and TNF-a) and alpha-defensin 1-3 were determined in blood and oral fluid by solid-phase immunoassay using test systems manufactured by Vector-Best (Novosibirsk, Russia). Statistical data processing was performed on a personal computer using standard software package for applied statistical analysis (Statistica for Windows v. 7.0). The $p<0.05$ value was used to assess the reliability of differences.

RESEARCH RESULTS

As is known, the spectrum of lesions of the oral cavity in various concomitant diseases is wide. At the same time, concomitant diseases contribute to the development of pathological conditions in the oral tissues, and on their background there are various drugs for their correction. Gerontological population, which is the main consumer of drugs, should not be ignored. When analyzing nosologies of gastrointestinal diseases, atrophic and chronic gastritis prevailed. According to the data obtained, 63% of patients with gastrointestinal pathology noted the presence of bad breath (halitosis). Dry mouth was mentioned by 28% of respondents. Changes in the color of the tongue and gums were noted by 52% of respondents. A burning sensation in the mouth was noted by 8% of respondents, and 12% of patients reported hyper-salivation. To determine the intensity of the carious process in patients with GIT pathology the KPU index was used. The KPU index in the patients was 8.48+0.91, which corresponds to the average level of caries intensity. The number of filled teeth ranged from 1 to 6. The number of extracted teeth was insignificantly lower than the number of filled teeth; it ranged from 1 to 24 teeth. CPU index values were significantly positively related to the diagnosis of GI nosology. The lowest values of the CPU index were in patients with chronic gastritis, and the highest values were in patients with IBDD. In addition to clinical examination of oral tissues, patients with GIT pathology underwent examination of mixed saliva, which reflects changes occurring in the oral cavity. The analysis of the results revealed some features of the cytokine profile in the mixed saliva of patients with gastrointestinal tract diseases As known, cytokines, having the ability to regulate the processes of cell proliferation, differentiation, functional activity, apoptosis, hematopoiesis, angiogenesis, as well as the ability to perform intercellular and intersystem interaction, determine the type, strength and duration of immune response, can have both pro- and anti-oncogenic effects. Their mechanism of action is realized in the extra- and/or intracellular way through binding to specific receptors located on the cytoplasmic membrane of cells or circulating in the soluble form. IL-1a and IL-1r are produced by activated macrophages, keratinocytes as inactive protein precursor molecules and are converted to active cytokines by either caspase-1 protease or IL-1-converting enzyme (1SE). The ability of IL-1r to inhibit gastric acid production is realized both directly, through its effect on receptors of parietal cells, and indirectly, through stimulation of PG E2 synthesis, which is a strong inhibitor of hydrochloric acid secretion, and through activation of receptors in the central nervous system located in the anterior hypothalamic region in the paraventricular nucleus.

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Our studies demonstrated an average 3.6-fold increase in concentrations of IL-1a in mixed saliva in patients with gastrointestinal diseases compared to healthy patients. High blood values of IL-1a in patients with gastrointestinal tract disease most likely indicate the development of a chronic inflammatory process. This condition is characterized by increased production of cytokines, which exhibit pro-inflammatory effects, i.e. cytokines in these pathological processes play the role of both aggressive and protective factors. Thus their maintenance depends on aetiological factor, a course variant, a stage, duration of chronic inflammatory and destructive disease. In response to chronic inflammation of gastrointestinal mucosa, there is induction of interleukin-8 secretion by macrophages. It is known that by activating neutrophils, IL-8 leads to their degranulation, release of lysosomal enzymes, leukotrienes, which have a damaging effect on the mucosa of the gastrointestinal tract. In addition, increased levels of IL-8 are also found in the peripheral blood, regardless of localization. In our studies, we observed a 3-fold increase of IL-8 level in mixed saliva in patients with gastrointestinal disease as compared to healthy individuals. Pro-inflammatory cytokine tumor necrotizing factor α (TNF-α) plays an important role in the formation of the inflammatory reaction. TNF-α is considered the strongest stimulus for IL-1β production and is synthesized by T lymphocytes and macrophages. This cytokine is multifunctional and plays a predominant role in the formation of local and general pathological processes, in particular it activates the synthesis of pro-inflammatory interleukins, stimulates T- and B-lymphocytes, regulates the intensity of inflammation, increases phagocytic activity of monocytes, nitric oxide formation, also involved in the physiological processes and inflammatory response in the gastroduodenal mucosa. As we can see from the presented findings, the level of tumor necrotizing factor α increased by 1,6 times in comparison with the parameters of the comparison group. Long-term and pronounced increase of TNF-a in mixed saliva in patients with gastroduodenal disease may contribute to imbalance between osteogenic function of osteoblasts and osteodestructive function of osteoclasts towards hyperactivation of the latter in dentition system.

CONCLUSIONS

Thus, increase of IL-4 level in this situation probably has compensatory character in relation to proinflammatory cytokines and acts as a factor stabilizing the course of the disease. Besides, it is pointed out that TNF-α and IL-6 levels can indirectly judge about activity of inflammatory process in gastroduodenal zone. The analysis of the obtained results, presented in Table 1, shows that the level of interleukin-4 in the mixed saliva of gastroduodenal disease patients is 23% lower than in the comparison group. At the same time, the level of IL-6 in the mixed saliva of the examined patients exceeded the initial level by 2.4 times. IL-6 is known to be an inducer of inflammatory reaction and triggers synthesis of acute phase proteins in the liver (C-reactive protein, serum amyloid A, etc.), as well as reduces production of fibronectin, albumin and transferrin in the liver. The key anti-inflammatory factor IL-10. is known to inhibit the production of TNFα, IL-1β and IL -6 and inhibit the expression of the major histocompatibility complex class II. One of the markers of inflammatory process activation is considered to be the level of antibacterial proteins defensins. We investigated the content of a-defensins (HNP1-3) in the saliva of patients with GIT diseases. As can be seen from the presented findings, the content of a-defensins 1-3 in the oral fluid of patients of the main group and healthy individuals presented in Table 1 indicates a decreased secretion of a-defensins 1-3 in the oral fluid of the main group

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relative to the indicators of the comparison group. The revealed factual material indicates inactivation of b-defensins, which can lead to increased microbial colonization and increase the risk of viral and bacterial infections in the oral cavity. Low levels of diphenzins in the mixed saliva of patients with GI disease contribute to a decrease in IL-8 secretion and progression of the process of inflammation in the oral mucosa. Thus, the study of cytokine and antimicrobial peptide content in mixed saliva of patients with GIT disease showed predominance of pro-inflammatory cytokines over anti-inflammatory ones and decrease of antimicrobial peptide level, which can activate bone tissue resorption. In general, the identified changes may lead to an imbalance in the local immune response of mucous membranes and the development of both autoimmune and inflammatory diseases of the oral cavity.

REFERENCES

1. Акбиева Д.С. Роль цитокинов в развитии заболеваний гастродуоденальной зоны // Современные проблемы науки и образования. – 2017. – № 2. С 64-69
2. Saperas E., Tache Y. Central interleukin-1 beta-induced inhibitionof acid secretion in rats: specificity of action. Life Sci. 1993;52: 785–792.
3. Sims J.E., Nicklin M.J., Bazan J.F., Barton J.L., Busfield S.J.,Ford J.E., Kastelein R.A., Kumar S., Lin H., Mulero J.J., Pan J.,Pan Y., Smith D.E., Young P.R. A new nomenclature for IL-1-family genes. Trends Immunol. 2001; 22: 536–537.
4. Novye chleny tsitokinov interleikina-1 i ikh rol' v destruktivnykhvospalitel'nykh zabolevaniyakh. Med. al'manakh. 2011;5 (18): 274–276.
5. . Ferrari D., Pizzirani C., Adinolfi E.. Lemoli R.M., Curti A.,IdzkoM., Panther E., Di Virgilio F. The P2X7 receptor:a key player in ИЛ-1 processing and release. J. Immunol. 2006;176: 3877–3883.
6. Казеко Л.А. Возможности диагностики заболеваний периодонта с использованием противомикробных пептидов слюны и десневой жидкости // Современная стоматология. - 2016. - №.1. - С.11-16.
7. Пантелеев П. В., Болосов И. А., Баландин С. В., Овчинникова Т. В. Строение биологические функции Р-шпилечных антимикробных пептидов. Журнал «АКТА НАТУРЭ»-2015. - Т. 7. - № 1 (24). - С.37-47.
8. Ali Adem Bahar, Dacheng Ren. Antimicrobial Peptides//Pharmaceuticals (MDPI). - 2013. - Vol.6 (12). - P.1543-1575.
9. Alexandre L. Pereira, Gilson C. Franco, Sheila C. Cortelli.. Influence of Periodontal Status and Periodontopathogens on Levels of Oral Human P-defensin-2 in Saliva // Journal of Periodontology.-2013. - V.84. - №1. - P.1445-1453.
10. Henrik Dommisch Soren Jepsen. Diverse Functions of Defensins and Other Antimicrobial Peptides in Periodontal Tissues //Journal of Periodontology. -2015.- V.69. - №1. - P.96-110.
11. Вавилова Т.П., Янушевич О.О., Островская О.Г. Слюна. Аналитические возможности и перспективы. М.: БИНОМ; 2014.
12. Будихина А.С., Пинегин Б.В. Дефензины — многофункциональные катионные пептиды человека. Иммунопатология, аллергология, ин- фектология. 2008;2:31-40.
13. Ericksen B, Wu Z, Lu W, Lehrer RI. Antibacterial activity and specificity of the six human alfa-defensins. Antimicrobial Agents and Chemotherapy. 2005;49(1):269-275.doi: 10.1128/AAC.49.1.269-275.2005.

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Publisher: The USA Journals

14. Abiko Y, Saitoh M, Nishimura M, Yamazaki M, Sawamura D, Kaku T. Role of в-defensins in oral epithelial health and disease. Medical Molecular Morphology. 2007;40(4):79-184.doi: 10.1007/s00795-007-0381-8.
15. Lehrer R.I., Lu W. a-Defensins in human innate immunity // Immunol. Rev. — 2012. — Vol. 245, N 1. — P. 84-112.
16. Гришин Д.В., Соколов Н.Н. Дефензины — естественные пептидные антибиотики высших эукариот // Биомедицинская химия. 2014. Т. 60. № 4. С. 438—447.
17. Gursoy U.K., Kononen E., Luukkonen N., Uitto V.J. Human neutrophil defensins and their effect on epithelial cells // J Periodontol. 2013. Vol. 84. P. 126—133
18. Пешкова Э.К., 2016; Пешкова Э.К. Морфофункциональная оценка особенностей зубочелюстного комплекса у больных с гипотиреозом и без патологии щитовидной железы: дис. ... канд.мед.наук /Э.К. Пешкова, ФГАОУ ВО «Белгородский государственный национальный исследовательский университет», Белгород, 2016. - 103 с.